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In the Supreme Court of the United States

OCTOBER TERM, 1972

No. 72-1686

DIANOVIN PHARMACEUTICALS, INC., a Corporation and NICOLAS O. CABRERO ORONOZ, an Individual,
PETITIONERS,

v.

UNITED STATES OF AMERICA.

PETITION FOR A WRIT OF CERTIORARI TO THE UNITED STATES COURT OF APPEALS FOR THE FIRST CIRCUIT AND REQUEST FOR SUMMARY REVERSAL

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The Petitioners, Dianovin Pharmaceuticals, Inc., and Nicolas O. Cabrero Oronoz pray that a Writ of Certiorari issue to review the judgment of the United States Court of Appeals for the First Circuit affirming an Order of the United States District Court for the District of Puerto Rico, rendered in these proceedings and request a Summary Reversal of the judgment.

Opinions Below

The opinion of the Court of Appeals, as yet unreported, appears at Appendix A, infra, p. 31. The Order of the United States District Court for the District of Puerto Rico, appears at Appendix B, infra, p. 37 and is reported at 342 F. Supp. 724.

Jurisdiction

The judgment of the United States Court of Appeals for the First Circuit was entered on March 16, 1973. See Appendix A, p. 31, infra. The judgment involves important state and territorial questions relating to federal law, not yet settled by this Honorable Court. This petition for Certiorari and Request for Summary Reversal was filed less than 90 days from the date aforesaid. The jurisdiction of this Honorable Court is invoked under 28 U.S.C. §§ 1254, 1651 and 2101.

Questions Presented

The United States Attorney in the Commonwealth of Puerto Rico in January of 1969 requested a permanent injunction be entered by the United States District Court for the District of Puerto Rico against petitioners for alleged violations of the Federal Food, Drug and Cosmetic Act, 21 U.S.C. 301, *et seq.*, specifically the prohibited acts contained under Title 21 U.S.C. 331 (a) and (k). Up to and including the proceedings that resulted in the consented to Permanent Injunction, petitioners were not represented by counsel nor was there an adversary hearing until much later.

Petitioners entered into a stipulation with an Assistant United States Attorney to lift the permanent injunction resulting in an order to that effect on June 29, 1970. The

Assistant United States Attorney later filed for an order to reinstate the Permanent Injunction. After an adversary hearing an order issued reinstating the permanent injunction. That order was affirmed on appeal. The questions thereby arising are:

1. Whether the action of the United States First Circuit Court of Appeals in affirming the lower court's order which determined it had jurisdiction over the subject matter and the petitioners was proper since,

   (a) Lack of jurisdiction can be raised at any time during proceedings.
   (b) Jurisdiction is not obtained by stipulation of the litigants.

2. Whether the determination that a manufactured pharmaceutical product is in interstate commerce because a raw material component was received in interstate commerce is contemplated by the Federal Food, Drug and Cosmetic Act, 21 U.S.C. 301, *et seq.*

3. Whether upon determining that a manufactured pharmaceutical or medicinal product is in interstate commerce because one or more of its component raw materials is received in interstate commerce and permitting Federal Food and Drug Administration's imposition of regulatory manufacturing norms on the entire manufacturing operation is Federal interference with and regulation of local manufacturing firms not in interstate commerce.

4. Whether the Prohibited Acts of the Federal Food, Drug and Cosmetic Act (21 U.S.C. 301, *et seq.*) under sections a and k (21 U.S.C. 331 (a) & (k)) apply to a finished medicinal product not in interstate commerce when these sections do not apply to an ingredient raw material received in interstate commerce.

5. Whether the "New Drug" definition of the Federal

Food, Drug and Cosmetic Act automatically excludes products as manufactured by petitioners.

Constitutional Provisions, Statutes and Rules Involved

This case involves the United States Constitution, the Federal Food, Drug and Cosmetic Act, 21 U.S.C. 301 *et seq.*, and the Code of Federal Regulations, Title 21, chapter 1 which read in pertinent part as follows:

United States Constitution Amendment X — Reserved Powers to States

The powers not delegated to the United States by the Constitution, nor prohibited by it to the States, are reserved to the States respectively, or to the people.

Federal Food, Drug and Cosmetic Act, Section 201

(21 U.S.C. 321) Definitions:

For the purposes of this chapter...

(a)(1) The term "State"... means any State or Territory of the United States, the District of Columbia, and the Commonwealth of Puerto Rico.

(2) The term "Territory" means any Territory or possession of the United States, including the District of Columbia and excluding the Commonwealth of Puerto Rico and the Canal Zone.

(b) The term "interstate commerce" means (1) commerce between any State or Territory and any place outside thereof...

(g)(1) The term "drug" means (A) articles recognized in the Official Homeopathic Pharmacopeia of the United States, or Official National Formulary, or any supplement to any of them; and (B) articles intended for use in the diagnosis, cure, mitigations, treatment, or prevention of disease in man or other animals; and (C) articles (other than food) intended to affect the structure or any function of the body of man or other animal; and (D) articles intended for use as a component of any articles specified in clause (A), (B), or (C) ...

(p) the term "new drug" means ...

(1) Any drug (except a new animal drug or an animal feed bearing or containing a new animal drug) the composition of which is such that such drug is not generally recognized, among experts qualified by scientific training and experience to evaluate the safety and effectiveness of drugs, as safe and effective for use under the conditions prescribed, recommended or suggested in the labeling thereof except that such a drug not so recognized shall not be deemed to be a "new drug" if any time prior to the enactment of this chapter, it was subject to the Food and Drug Act of June 30, 1906, as amended, and if at such time its labelling contained the same representations concerning the conditions of its use; or

(2) Any drug (except a new animal drug; an animal feed bearing or containing a new animal drug) the composition of which is such that such, as a result of investigations to determine its safety, and effectiveness for use under such conditions, has become so recognized, but which has not, otherwise that in such investigations, been used to a material extent or for a material time under such conditions.

PROHIBITED ACTS

Section 301 (21 U.S.C. 331)

The following acts and the causing thereof are prohibited:

(a) The introduction or delivery for introduction into interstate commerce of any food, drug, device or cosmetic that is adulterated or misbranded.

(g) The manufacture within any Territory of any food, drug, device, or cosmetic that is adulterated or misbranded.

(k) The alteration, mutilation, destruction, obliteration or removal of the whole or any part of the labeling of, or the doing of any other act with respect to, a food, drug, device or cosmetic, if such act is done while such article is held for sale (whether or not the first sale) after shipment in interstate commerce and results in such article being adulterated or misbranded.

FACTORY INSPECTION

Section 704(a) For purposes of enforcement of this Act, officers or employees duly designated by the Secretary, upon presenting appropriate credentials and a written notice to the owner, operator, or agent in charge, are authorized (1) to enter at reasonable times, any factory, warehouse, or establishment in which food, drugs, devices, or cosmetics are manufactured, processed, packed, or held, for introduction into interstate commerce or after such introduction, or to enter any vehicle being used to transport or hold such food, drugs, devices, or cosmetics in interstate commerce; and (2) to inspect, at reasonable times and within reasonable limits and in a reasonable manner, such factory, warehouse, establishment, or vehicle and all pertinent equipment finished and unfinished materials, containers and labeling therein. In the case of any factory, warehouse, establishment or consulting laboratory in which

prescription drugs are manufactured, processed, packed or held, inspection shall extend to all things therein (including records, files, papers, processes, controls, and facilities) bearing on whether prescription drugs which are adulterated or misbranded within the meaning of this Act, or which may not be manufactured, introduced into interstate commerce, or sold, or offered for sale by reason of any provision of this Act, have been or are being manufactured, processed, packed, transported or held in any such place, or otherwise bearing on violation of this Act. No inspection authorized for prescription drugs by the preceding sentence shall extend to (A) financial data, (B) sales data other than shipment data, (C) pricing data, (D) personnel data (other than data as to qualifications of technical and professional personnel performing functions subject to this Act), and (E) research data (other than data, relating to new drugs and antibiotic drugs, subject to reporting and inspection under regulations lawfully issued pursuant to section 505 (i) or (j) of section 507 (d) or (g) of this Act, and data, relating to other drugs, which in the case of a new drug would be subject to reporting or inspection under lawful regulations issued pursuant to section 505 (j) of this Act.)

CODE OF FEDERAL REGULATIONS

Revised as of January 1, 1970

Title 21 — Chapter 1

Subpart — A Procedure and Interpretative Regulations.

130.1 Definitions and Interpretations:

As used in this part:

(a) ...

(b) ...

(g) ..."New Drug substance" means any substance that when used in the manufacture, processing, or packing of a drug, causes that drug to be a new drug, but does not include intermediates used in the synthesis of such substance.

(h) The newness of a drug may arise by reason (among other reasons) of: (1) The newness for drug use of any substance which composes such drug, in whole or in part, whether it be an active substance or a menstrum, excipient, carrier, coating, or other component, (2) The newness of drug use of a combination of two or more substances, none of which is a new drug, (3) The newness for drug use of the proportion of a substance in a combination, even though such combination containing such substance in other proportion is not a new drug, (4) The newness of use of such drug in diagnosing, curing, mitigating, or treating, or preventing a disease, or to affect a structure or function of the body, even though such drug is not a new drug when used in another disease or to affect another structure or function of the body, (5) The newness of a dosage or method or duration of administration or application or other condition of use prescribed, recommended, or suggested in the labeling of such drug, even though such drug when used in other dosage, or other method or duration of administration or application, or different condition is not a new drug.

Statement of Facts

DIANOVIN PHARMACEUTICALS, INC. was founded and organized under the laws of the Commonwealth of Puerto Rico in the year 1953. Since that time it dedicated itself to the manufacture of pharmaceutical products for local consumption only, that is sales within Puerto Rico, such sales being handled by Dianovin itself. The President of the Corpo-

ration, Mr. Nicolas O. Cabrero Oronoz, is a graduate pharmacist from the school of pharmacy of the University of Puerto Rico, who obtained his degree on November 10, 1949. His license number 885 is recorded in the Registry kept by the Board of Pharmacy of Puerto Rico at Volume 6 page 171.

A complaint for injunction was filed on January 16, 1969 by the United States Attorney in Puerto Rico to enjoin and restrain Petitioners from violating the Federal Food, Drug and Cosmetic Act, (21 U.S.C. 301 *et seq.*) specifically Title 21 U.S.C. 331 (a) and (k). A temporary restraining order was granted on January 20th, 1969 and on February 17, 1969 a Permanent Injunction followed. At those hearings Petitioners were not represented by counsel.

Petitioners filed a "Motion to Dissolve Injunction" in late October 1969 which was denied — as per order of December 14, 1969.

Again on April 30, 1970 Petitioners requested dissolution of the Injunction. On June 11, 1970 Petitioners and Assistant United States Attorney entered into a stipulation suspending the Injunction. Pursuant to the stipulation an order was issued on June 29, 1970 lifting the permanent injunction.

The Assistant United States Attorney filed for and obtained an order to reinstate the order of Permanent Injuntion on February 17, 1971. No hearing of any sort was held nor were Petitioners notified of the Motion requesting reinstatement of the Injunction. The order was set aside and during a hearing held on May 4, 5 and 6, 1971 the Assistant United States Attorney presented evidence to attempt to establish reasons why the permanent injunction should be reinstated. Petitioners also presented evidence and filed motions requesting dismissal.

On May 3, 1972 an Order was filed and entered reinstating the Permanent Injunction. That order was affirmed on

appeal and the affirmation is hereby requested to be reviewed on Certiorari.

Reasons for Granting the Writ

Petitioners respectfully contend that the decision rendered by the Honorable United States Court of Appeals for the First Circuit, among other things, deals with a very important state and territorial matter insofar as a Federal Agency, e.g., the Food and Drug Administration, imposes its norms and regulations upon a manufacturing firm that is outside of its jurisdiction, thereby going beyond its powers and creating a conflict of powers between State and Federal Governments. By so doing the Federal Food and Drug Administration deprives such affected parties of their Constitutional rights, not given to Congress nor prohibited to the states and so reserved to the states or to the people.

I. Two Jurisdictional Aspects Not Decided in Accord With Applicable Decisions of This Court.

(a) *Lack of jurisdiction can be raised at any time during proceedings.*

An objection to the jurisdiction of a court based on the absence of jurisdiction over the subject matter must be considered and may be effectively raised at any time. (*Gainesville* v. *Brown-Crummer Investment Co.*, 277 U.S. 54, 74 L. ed. 781, 48 S. Ct. 454). This principle goes even further since as a general rule it is accepted and this Honorable Court has established that proceedings conducted or decisions made by a court are legally void where there is an absence of jurisdiction over the subject matter. (*Re Bonner*, 151 U.S. 242, 38 L. ed. 149, 14 S. Ct. 323).

According to the decision entered by the Court of Appeals the only narrow issue before the District Court was whether there were present any of the conditions provided in the June 29, 1970 order, as causing a reversion of the injunction. The reason why that issue alone was to be considered was that there must be progress in litigation.[1] It sounds as if it is more important to put an end to litigation than to consider difficult issues and do justice.

The opinion goes on to say, and we quote from the third paragraph of page three of the opinion,

> "Only after the hearing did appellants raise 'jurisdictional' objections, based primarily upon the government's failure to show that the vitamin K for injection entered interstate commerce after manufacture. The short answer is that the government had no reason at the hearing to do so . . ."

The subject matter here involved is precisely the applicability of the Federal Food, Drug and Cosmetic Act, supra, to affirm manufacturing products not intended for or in interstate commerce and its applicability to one product, vitamin K injectable, not in interstate commerce.

The United States First Circuit Court of Appeals did not consider the objection to the jurisdiction. It goes on to say at the top of page four of its opinion as follows,

> "We do not say that the injunction would be reinstated by showing the mishandling of some previously unmentioned drug over which the court clearly lacked jurisdiction. But Menadione Sodium Bilsulfite injection was one of the drugs complained of in the original 1969 proceeding, where jurisdiction was con-

[1] Opinion of the United States First Circuit Court of Appeals at page 3 first paragraph (Appendix A, p. 33).

ceded. The government, on its reinstatement motion, had no duty whatever to reestablish the interstate connections of the drug; at the very most, if appellants, at this late date, had wished to raise a jurisdictional defense, the burden of proving the necessary facts was theirs".

A look at the record shows clearly that through the government's own witnesses it was shown that there was no interstate commerce of the manufactured vitamin K injectable. The issue of lack of jurisdiction over the subject matter was not, therefore, considered. It was not considered because as the Circuit Court opines, jurisdiction had been conceded and the objection was raised after hearing. Yet during the hearing Mr. Cabrero stated and we quote from the stenographic transcript of the evidentiary hearing in the District Court, Appendix on Appeal at page 205, line 18, as follows,

"Q. Tell me, Mr. Cabrero, do you recall in the testimony the fact that the representatives of the Food and Drug had gone to your place, or to Dianovin plant to carry out inspections on the eighteenth and various days after that of November 1970.

A. That's something I have always, I mean I think they have gone there although I object. I let them come in into the laboratory although I am almost sure it's against my will because I am almost sure that they did not have any jurisdiction to go into my place. And every time they go into my place I think they are violating not only my Constitutional rights, but I think also they are violating the constitution of the United States because this law—the Food and Drug Act was established to control the channels of com-

merce, that is, of interstate commerce and if I do not manufacture for interstate commerce they just don't have any jurisdiction over me."

The question of jurisdiction, therefore, was raised during the evidentiary hearing whence the District Court disregarded the objection to the jurisdiction as did later the Appeals Court. Even if ithe objection to jurisdiction was raised in a written motion after the hearing as it had to be done because the District Court did not consider the matter when it was raised during the hearing, the objection was raised before judgment was entered. Nevertheless objections to jurisdiction based on the absence of jurisdiction over the subject matter may be effectively raised at any time and even for the first time on appeal. (*Panhandle Eastern Pipe Line Co.* v. *Federal Power Commission,* 324 U.S. 635, 89 L. ed. 1241, 65 S.Ct. 821).

We very respectfully contend the jurisdictional objection was effectively raised.

(b) *Jurisdiction is not obtained by stipulation of the litigants.*

The term jurisdiction here was used with reference to the power or authority of a Federal Agency over local manufacturing firms not in interstate commerce, over the products themselves and the exercise of power or authority of the Federal Courts over the subject matter.

The source of jurisdiction here, if any, is legislative. We must look to the Federal Food, Drug and Cosmetic Act, 21 U.S.C. 301 *et seq.* to determine if it applies to local pharmaceutical manufacturing firms not in interstate commerce, to determine if it applies to a manufactured pharmaceutical or medicinal product not in interstate commerce

and then the court must determine if it had jurisdiction over the subject matter.[2]

The source of that jurisdiction of the agency or of the court does not rest on stipulations of the litigants as one might construe from the opinion rendered by the United States Court of Appeals for the First Circuit, when it says at page three, last paragraph,

> "Only after the hearing did appellants raise 'jurisdictional' objections, based primarily upon the government's failure to show that the vitamin K for injection entered interstate commerce after manufacture. The short answer is that the government had no reason at the hearing to try to do so. Jurisdiction had long before been settled—by the district court's 1969 findings that drugs were distributed, and components received, in interstate commerce, from which the appellants did not appeal, and by the consented-to order of permanent injunction which recited that the court 'has jurisdiction of the subject matter herein and of all persons or parties hereto.' "

What was not given any importance or mention was that the 1969 findings were based on a one-sided hearing where Dianovin Pharmaceuticals, Inc. and its president were not represented by counsel and where we feel an adversary hearing should have been held upon the court's own insistence for reasons akin to the principle of defendants' right to counsel in other type of proceedings which we do not here discuss. It is mentioned, however, to show that the stipulation or conceded-to permanent injunction was not so firm

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[2] 20 Am. Jur. 2d, Section 92 quoting from *Texas & P. R. Co. v. Gulf, C. & S.F.R. Co.*, 270 U.S. 266, 70 L. ed.. 578, 46 S.Ct. 263 and other cases says, "a court has the power and duty to examine and to determine whether it has jurisdiction of a matter presented to it . . ."

or dependable even if it were held as controlling in determining the existence or non-existence of jurisdiction.

Regardless of the facts and the proceedings which led to the stipulations and the conceded-to permanent injunction, such arrangements between litigants cannot confer jurisdiction to the Federal Food and Drug Administration or to the Court if the Federal Food, Drug and Cosmetic Act, supra does not confer jurisdiction powers upon these entities. We contend that as evidenced by the uncontested facts the Federal agency and the Federal Courts here involved are not conferred jurisdiction by either the Federal Food, Drug and Cosmetic Act or the United States Constitution making the proceedings conducted and the decisions rendered legally void. (*Re Bonner,* supra)

II. Whether the Determination That a Manufactured Pharmaceutical Product Is In Interstate Commerce Because a Raw Material Component Was Received in Interstate Commerce Is Contemplated by the Federal Food, Drug and Cosmetic Act, 21 U.S.C. 301, *et seq.*

The Federal Food, Drug and Cosmetic Act, supra, rests upon the constitutional power of Congress to regulate interstate commerce. This Honorable Court, in addition, has said that Congress seeks to keep interstate channels free from deleterious, adulterated and misbranded articles of specified types to the end that public health and safety might be advanced. (*U. S.* v. *Walsh*, Col. 1947, 331 U.S. 432; 91 L. ed. 1585; 67 S. Ct. 1283).

Interstate Commerce has always been a requirement when applying the Federal Food, Drug and Cosmetic Act to foods, drugs, cosmetics, devices or the firms that elaborate the products involved simply because Congress has no power to regulate any other type of commerce. By defini-

tion, and included in the Act, articles received from foreign areas or countries, that is from outside of the United States are considered to be in interstate commerce.

A clear distinction between commerce and manufacturing was made in *Acme, Inc.* v. *Besson,* 10 F Supp. 1.

> "Manufacture is transformation the fashioning of raw material into a change of form for use. The functions of commerce are different. The buying and selling and the transportation incidental thereto constitute commerce."

The Court went on to say that,

> "Commerce has no power under the Constitution to regulate manufacture within a state, though interstate commerce in a broad sense may be thereby affected."

There is nowhere to be found in the Federal Food, Drug and Cosmetic Act any provisions regulating manufacturing within any state. The Commonwealth of Puerto Rico for the purposes of the Act is defined as a state and excluded as a Territory. (21 U.S.C. 321 Definitions).

Under the section covering prohibited acts we find that the manufacture within any Territory of any food, drug, device or cosmetic that is adulterated or misbranded is a prohibited act.[3] Such a provision can not be made extensive to states because as we have said the regulating of manufacturing is a power not delegated to the United States

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[3] Food, Drug and Cosmetic Act—Prohibited Acts—Section 301 (21 U.S.C. 331)

The following acts and the causing thereof are prohibited:

(a) . . .

(b) . . .

(g) The manufacture within any Territory of any food, drug, device or cosmetic that is adulterated or misbranded.

by the Constitution, nor prohibited by it to the States and consequently is reserved to the states or to the people. (United States Constitution, Amendment X).

The United States Court of Appeals for the First Circuit was aware of the nonexistence in the Federal Food, Drug and Cosmetic Act of any provision regulating manufacturing within a state. Petitioners had raised the issue. The Court decided first that the raw material vitamin K utilized in the production of vitamin K injectable received in interstate commerce did not undergo any change, transformation or manufacturing. The opinion at the middle of page four states,

> "Even, however, on the conceded facts relating to the interstate connections of vitamin K for injection, appellants' jurisdictional argument fails. It is undisputed that the raw material vitamin K utilized in the production of vitamin K injectable was received in interstate commerce. Following a commonly-known formula, appellants would mix the ingredients with liquid and place the resulting solution in ampules for sale."

The record will show there was no commonly-known formula followed by petitioners and least of all, one that required mixing of ingredients with liquid. An uncontested and conceded fact is that Dianovin Pharmaceuticals, Inc., is a manufacturing firm selling its pharmaceutical or medicinal manufactured products in the local market only. We can not change the facts. Of course the raw material vitamin K in powder, granules or whatever solid form is received in interstate commerce. In that form it is not found in the United States Pharmacopeia. It must still be transformed or changed through a manufacturing process and encased in ampules before being sold locally as a finished pharmaceutical or medicinal product. That process

can not be called mixing and the government conceded it was manufacturing.

There can be no inference from the Federal Food, Drug and Cosmetic Act that because one component raw material is received in interstate commerce the resulting manufactured product is also considered as being in interstate commerce.

The doctrine has been the result of interpretations by various United States Courts of Appeals in cases involving foods, drugs and devices. In all the cases interstate commerce was first established. To apply the principle that if a part of the whole product is in interstate commerce, the entire product is also in interstate commerce the various courts determined that mixing was involved and not manufacturing or that the ingredient did not lose its identity.

United States v. *Cassaro, Inc.*, 443 F. 2d. 153 (1st Cir. 1971)

For this particular case *United States* v. *Cassaro, Inc.* was said to be controlling.[4] In that case flour, received in interstate commerce and made into bread and rolls for local sale, was adulterated after entering interstate commerce. Based on *United States* v. *Krumm*, 269 F 848 (E.D. Pa. 1921) and the Food, Drug and Cosmetic Act, flour was defined as a food, a finished product. It was still the same product after it was processed and made into bread and rolls. There, no manufacturing took place. Bread and rolls are not manufactured products. Besides we respectfully submit that food products because of their nature and the interest of the Federal Government within its supervisory functions over interstate commerce must be considered dif-

[4] At top of page 5 of the Opinion of the United States Court of Appeals for the First Circuit (Appendix A, p. 35).

ferently under the Federal Food, Drug and Cosmetic Act.[5]

We believe all the cases cited in footnote 5 of the Opinion of the United States First Circuit Court of Appeals can be distinguished.

> *United States* v. *39 Cases . . . Mich. Brand Korleen Tablets,* 192 F. Supp. 51 (E.D. Mich. 1961) *affirmed sub nom. United States* v. *Detroit Vital Foods, Inc.,* 330 F.2d 78 (6th Cir. 1964), *cert. den.,* 379 U.S. 832 (1964).

Korleen Brand Tablets were manufactured in Michigan for distribution in Michigan and were subject to the Federal Food, Drug and Cosmetic Act because the tablets were composed of finished drugs found in and recognized in the official United States Pharmacopoeia, official Homoeopathic Pharmacopoeia of the United States or official National Formulary or any supplement to any of them. The representations made in leaflets circulated in connection with the sale of the product not only demonstrated that the tablets were "drugs" within the statutory definition, but were proclaimed to the public as having therapeutic value not as a tablet, but each component drug individually was proclaimed as having certain therapeutic value. The claim with regard to the individual finished drug components proved these had not lost their identity. The Court distinguished the case from *United States* v. *An Article or Device Consisting of 31 Units,* (D.C.E.D. Mich. 1950) 180 F. Supp. 52 and *United States* v. *40 Cases, More or Less,* (D.C. N.D. N.Y. 1960) 188 F. Supp. 290. In both cases the Court held that an article or device is not subject to the jurisdiction of the Federal Food, Drug and Cosmetic Act where the only components shipped in interstate commerce were either a minor ingredient of the final product or several commonly used components which

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[5] *United States* v. *40 Cases . . . Pinocchio Brand 75% Corn . . . Oil,* infra.

lost their identity within the newly manufactured device. The Court said that,

> "In contrast, in the case at bar, the 'drugs' comprising the Korleen Tablets are the very heart of the manufactured and tableted 'drug' and were proclaimed as such to the public."

Dianovin Pharmaceuticals, Inc., is not making any claim with regard to the ingredient raw material and as received, the ingredient raw material is not to be found as a recognized drug in any of the official compendia. It is not a finished drug component and therefore it can not be subject to adulteration as an ingredient.

> *United States* v. *Detroit Vital Foods, Inc.*, 330 F.2d 78 (6th Cir. 1964) *cert. den.* 379 U.S. 832 (1964)

The very same situation existed in this case as in *United States* v. *39 Cases . . . Mich. Brand Korleen Tablets, supra.* In fact the product involved here again is Korleen Brand Tablets.

Claims were made with regard to the ingredient drugs which were fraudulent and misleading. These claims were made with respect to the component drugs themselves which were recognized and listed in the official United States Pharmacopeia or the official National Formulary. These ingredients, as finished drugs did not lose their identity in the combination to form the tablets as the very representations in leaflets circulated with the sale of the tablets demonstrated.

No misleading or fraudulent claims can be attributed to Dianovin Pharmaceuticals, Inc. or to Mr. Nicolas O. Cabrero Oronoz with regard to the ingredient raw material. The ingredient raw material is not a drug recognized in

any of the official U.S.P. or National Formulary. The evidence shows that a manufacturing firm in its manufacturing process changes a raw material from an unusable form to a product fit for human use.

United States v. *40 Cases . . . Pinocchio Brand 75% Corn . . . Oil,* 289 F.2d 343 (2nd Cir. 1961) *cert. den.* 368 U.S. 831 (1961)

Several vegetable oils were combined. It was argued that such processing created a new product which was different from the ingredient oils that had been shipped in interstate commerce. The Court overruled that contention saying:

> "We would be undermining the remedial legislative purpose of consumer protection were we to deny the power to seize misbranded articles on the ground that such foods as corn oil, peanut oil, soya bean oil and olive oil when mixed constitute a different product from a blend of less than all or from a pure measure of any one of them.
>
> "The oils were finished food products shipped in interstate commerce from different states of the Union and from foreign countries. These finished products, oils, were blended in the state of New York to be sold within that state. The blend was then packed by A.M.S. Packaging Company of New York in one gallon cans, six cans in a case and branded "Pinochio", labeled '25 per cent pure olive oil'. An examination showed that the cans contained little or no olive oil,"

The Court says further on;

> "In enacting the 1948 amendment to the Pure Food, Drug and Cosmetic Act, Congress sought to fill the

gap in the regulatory scheme pointed out in United States v. Phelps Dodge Mercantil Co., supra, by subjecting to condemnation food which had been adulterated or misbranded after coming to rest within a state but before being sold to a consumer. The interest of the Federal Government in ensuring that such food meets minimum standards of purity and is not misbranded arises out of its supervisory function over interstate commerce. The House and Senate reports both referred expressly to the Congressional desire to protect the integrity of interstate products so as not to depress the demand for goods that must travel across state lines."

The Court goes on to state:

"This interest surely extends to products such as olive oil, which a New York consumer would probably recognize as out-of-state or foreign in origin.

"Moreover in this case all the components of the oil blend had been transported in interstate commerce, and the completed mixture was being held for sale as 'oil' the very type of food which had traveled across the state line. This is not a case in which oil which was transported interstate was used as one of many ingredients in a finished product which in no way resembled the food which had crossed state lines."

Still further on the Court also states,

"Congress surely intended the provisions of the Food, Drug and Cosmetic Act to apply to foods processed within a state, after shipment in interstate commerce, as was the case here. The statute must be

> read and applied broadly in order to effectuate its remedial purpose * * * . . . We have no doubt of the power of Congress so to protect the public with respect to foodstuffs which have been shipped in interstate and foreign commerce".

Our case does not involve a finished food product for which Congress has intended special application due to the nature of finished food products. Petitioners respectfully contend that if a pharmaceutical or medicinal product were involved, manufactured from various raw materials, all shipped in interstate commerce, and that resultant manufactured product is not sold in interstate commerce, the principle set forth in *United States* v. *40 Cases . . . Pinocchio Brand 75% Corn . . . Oil, supra,* could not apply. Finished food products used as ingredients in other food products undergo processing and not manufacturing. In pharmaceutical products manufacturing is involved and seldom is there mixing, blending or processing. Here, manufacturing is involved.

Palmer v. *United States,* 340 F.2d 48 (5th Cir. 1964) *cert. den.* 382 U.S. 903 (1965)

In *Palmer* v. *United States,* the article of drug was not a drug manufactured within the state of Texas where the cause of action arose but rather was manufactured in Greenville, South Carolina. Interstate commerce was definitely established. The defendant in that case was a druggist and not a manufacturer. Another important difference between that case and the present one is that there an amphetamine drug was involved while here it is a vitamin. Amphetamines are now outside of the jurisdiction of the Federal Food, Drug and Cosmetic Act (Drug Abuse Control Amendment of 1965 and are treated differ-

ently. The principles now applicable to stimulants or depressants are not applicable to vitamins.

United States v. *Allbrook Freezing & Cold Storage, Inc.*, 194 F.2d 937 (5th Cir. 1952)

Here the government alleged that fresh strawberries had been adulterated while being processed and then shipped in interstate commerce. There were allegedly about 1000 cans, in whole or in part of decomposed and filthy substance moldy and rotten berries shipped in interstate commerce from Louisiana to Mississippi and there packaged with sugar added. The District Court dismissed for lack of jurisdiction and the Appeals Court reversed and remanded so the libel be heard on its merits.

The Appeals Court held that even though the Act provides that no definition or quality of fresh fruits shall be established, that does not preclude condemnation and seizure of shipments of strawberries, if adulterated and that fact that after the strawberries were frozen and canned, they had not been introduced into interstate commerce did not make their seizure premature.

The fresh strawberries had been shipped in interstate commerce to begin with and were adulterated while being processed. Here again no manufacturing took place and the strawberries are food received initially in interstate commerce as a finished product.

Dianovin Pharmaceuticals, Inc. did not receive a finished product least of all a food and adulterate it. What is sought against Dianovin Pharmaceuticals, Inc. and its president is an injunction affecting its entire manufacturing operation as opposed to seizure and condemnation of a particular product.

So it is that while the principle that if a part of the whole is received in interstate commerce the whole is also

considered as being in interstate commerc has been sustained in some cases, special conditions have existed.

We have noted from the cases discussed above what these conditions are and none can be said to confirm that a manufactured pharmaceutical or medicinal product is in interstate commerce because a raw material component was received in interstate commerce. Even under its broadest interpretation, the Federal Food, Drug and Cosmetic Act supra, does not contemplate the principle.

III. Whether the Determination that a Manufactured Pharmaceutical or Medicinal Product Is in Interstate Commerce Because One or More of its Component Raw Materials Is Received in Interstate Commerce and Permitting Federal Food and Drug Administration's Imposition of Regulatory Manufacturing Norms on the Entire Manufacturing Operation Is Federal Interference With and Regulation of Local Manufacturing Firms Not in Interstate Commerce.

In attempting to obtain re-imposition of the injunction against Petitioner's entire operation the government tried to show that Federal regulations with regard to "Good manufacturing Practices" were not complied with. It follows, of course, that if a firm manufactures for shipment in interstate commerce, it must meet the Federal requirements.

Petitioners products are not sold in interstate commerce and are definitely manufactured within the Commonwealth of Puerto Rico. By the fiction that if a component raw material is in interstate commerce the entire manufactured product also is in interstate commerce a conflict is created. The Federal government then is permitted to regulate local manufacturing which is in conflict with the United

States Constitution. That power is not delegated to the United States nor prohibited by it to the States so that it is reserved to the states or to the people.

The Commonwealth of Puerto Rico is called upon to act under its own Food, Drug and Cosmetic Act if such pharmaceutical products, manufactured within its boundaries and sold therein are found to be adulterated, misbranded or in some other fashion not in comformity with the Commonwealth Law.

Petitioners understand that is the practice in the rest of the United States and see no reason why it should not be so in Puerto Rico.

In addition to the above, in attempting to obtain reimposition of the injunction over Petitioner's entire operation on the alleged one manufactured product being defective, there is interference with a local manufacturing firm. The evidence showed that Food and Drug Inspectors entered the premises of Dianovin Pharmaceuticals, Inc., assuming they had jurisdiction. Under section 704, Factory Inspections (21 U.S.C. 374) inspectors are authorized to enter factory, warehouse or establishments in which drugs are manufactured for introduction into interstate commerce or after such introduction. Inspection of such areas or places is also allowed, but always when the required interstate commerce is met.

Petitioners very respectfully contend that because of the inspections carried out the imposition of the "Good Manufacturing Practices" and other Federal regulations as a condition not to re-instate an injunction is Federal interference with and regulation of a local manufacturing firm not in interstate commerce. At most, if the government proved that one product is covered by the Federal Food, Drug and Cosmetic Act and that it was adulterated or misbranded, then it could seize the product and request its destruction. It could not and should not be allowed, in

conflict with the "Supreme Law of the Land" to obtain an injunction and thereby interfere with and regulate the entire manufacturing operation of a local firm not in interstate commerce.

IV. Whether the Prohibited Acts of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 301, *et seq.*) Under Sections A and K (21 U.S.C. 331 (a) & (k)) Apply to a Finished Medicinal Product Not in Interstate Commerce When These Sections Do Not Apply to an Ingredient Raw Material Received in Interstate Commerce.

Section (a) of the Prohibited Acts does not allow the introduction or delivery for introduction into interstate commerce of any food, drug, device or cosmetic that is adulterated or misbranded.

Section (k) of the Prohibited Acts does not allow the alteration, mutilation, destruction, obliteration, or removal of part or all of the labeling or the doing of any other act to a food, drug, device or cosmetic while it is being held for sale, whether or not the first sale, after shipment in interstate commerce and results in such article being adulterated or misbranded.

Both sections presuppose the doing of an act, which results in the adulteration or misbranding of a drug, the first before its introduction or delivery for introduction into interstate commerce and the other while the drug is held for sale whether or not the first sale after shipment in interstate commerce.

A raw material drug in interstate commerce or delivered for such introduction must not be adulterated or misbranded and if it were falls under section (a) of the Prohibited Acts as well as section (k).

On the other hand that same raw material received in interstate commerce to be used in a manufacturing process which transforms it can not fall under the mentioned prohibited acts because it no longer exists as originally received. It has lost its identity and having ceased to exist no act can be done which would result in its adulteration or misbranding.

We have already discussed cases where ingredient drugs did not lose their identity, were finished products in themselves and were subject to the Prohibited Acts.[6]

Raw material drugs received in interstate commerce from outside of the United States are inspected at the port of entry. If found adulterated or misbranded, the raw material drugs would not be allowed to enter the Country.[7]

It seems obvious that section (a) of the Prohibited Acts does not apply to a raw material ingredient already admitted into the country to be used in a local manufacturing operation which transforms the ingredient raw material. If the "new product" should enter interstate commerce section (a) would apply to that different product which must not be adulterated or misbranded.

Neither does section (k) apply to such a raw material ingredient already adimitted into the country to be used in a local manufacturing operation and where the particular raw material ingredient is not being held for sale after such shipment. The raw material ingredient now does not exists and if it is still being held it is for use in the manufacture of another product.

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[6] *United States* v. *39 Cases . . . Mich. Brand Korleen Tablets* and *United States* v. *Detroit Vital Foods, Inc.*, previously discussed.

[7] Mr. Charles A. Wayne, Assistant to the National Director for Drug Affairs testified to those effects and that testimony appears at page 167 line 5 to page 168 line 4 of the Appendix on Appeal.

V. Whether the "New Drug" Definition of the Federal Food, Drug and Cosmetic Act, Automatically Excludes Products as Manufactured by Petitioners.

The "New Drug" definition in the Federal Food, Drug and Cosmetic Act (21 U.S.C. 321, (p) (1)) and the definition given in the Code of Federal Regulations, Title 21 Chapter 1 subpart A-130.1 (g), (h) establish what a new drug is. It is sufficient that dosage is changed, usage differs from previous usage, that the proportion of substances in the drug differs, that the above is shown on the labeling, even though the same drug when used otherwise is not a new drug.

Any manufacturing firm that has received raw materials in interstate commerce and manufactures pharmaceutical drugs, it would follow, is not subject to the Federal Food, Drug and Cosmetic Act unless the product is to be shipped in interstate commerce. If it should change the use of a product already in interstate commerce or make any of the changes given in the definition of a new drug, the firm must obtain a "new drug application" before the product may be sold or shipped in interstate commerce.

Not only is the requirement an additional safeguard in keeping the channels of interstate commerce free of undesired products but it also helps in classifying various products in interstate commerce by their use among other classifications. By requiring the new drug application the Food and Drug Administration is also made aware of manufacturing firms with intentions to sell or ship their products in interstate commerce.

Products manufactured by Dianovin Pharmaceuticals, Inc., would automatically be excluded from the Federal Food, Drug and Cosmetic Act. In order for such products to fall under the Federal jurisdiction a "new drug ap-

plication" must be obtained to allow their sale or shipment in interstate commerce. Since no sale or shipment in interstate commerce is intended or carried out, the "new drug" concept in the Federal Food Drug and Cosmetic Act excludes Petitioner's products.

Conclusion

For the reasons stated above, it is respectfully submitted that this petition for certiorari should be granted.

This Honorable Court should also summarily reverse the decision of the Court below to maintain the separation of powers between the legislative, judicial and executive branches of government, to keep the Federal government from infringing on states rights and to uphold the Constitution of the United States as the Supreme Law of the Land.

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APPENDIX A

United States Court of Appeals
For the First Circuit

No. 72-1326

UNITED STATES OF AMERICA,

PLAINTIFF, APPELLEE,

v.

DIANOVIN PHARMACEUTICALS, INC., et al.,

DEFENDANTS, APPELLANTS.

APPEAL FROM THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF PUERTO RICO

Before COFFIN, *Chief Judge*,
McENTEE and CAMPBELL, *Circuit Judges*.

Frank Carbo for appellants.
Howard S. Epstein, Attorney, Antitrust Division, Department of Justice, wth whom *Thomas E. Kauper*, Assistant Attorney General, Antitrust Division, *Julio Morales Sanchez*, United States Attorney, *Gregory B. Hovendon*, Chief, Consumer Affairs Section, *Alvin L. Gottlieb*, Deputy Assistant General Counsel, *Joanne S. Sisk*, Chief, Appellate and Special Proceedings Branch, and *Jeffrey B. Springer*, Attorney, were on brief, for appellee.

March 16, 1973

CAMPBELL, *Circuit Judge*. This is an appeal by a Puerto Rico drug manufacturer, Dianovin, and its president, from an order of the district court[1] reinstating its earlier permanent injunction restraining them from activities violative of the Federal Food, Drug and Cosmetic Act (the "Act").[2]

Appellants' principal contention is that the district court lacked jurisdiction, there having been no showing at the

[1] *United States* v. *Dianovin Pharmaceuticals, Inc.*, 342 F.Supp. 724 (D. P. R. 1972).
[2] 21 U.S.C. § 301 *et seq.*

hearing on reinstatement of the injunction that the drug there in issue (vitamin K for injection) entered interstate commerce after its manufacture by Dianovin. They assert further that Congress may not regulate what they describe as a local manufacturer solely manufacturing for local consumption, and that the drugs manufactured were "new drugs". Finally, assuming jurisdiction, they say the evidence was insufficient to warrant the injunction. We affirm.

This is not an appeal from an original injunction. The proceeding and order before us were upon a motion of the United States Attorney, made on February 5, 1971, to reinstate a permanent injunction which originally was entered against the appellants on February 17, 1969. The earlier injunction had been entered after hearing and was with the consent of the defendants.[3] Thereafter, on June 29, 1970, in an order entered by the district court (reciting the consent of all parties including the appellants, who appeared through counsel), the original injunction was suspended until further order of the court, its terms to "revert to their full force and effect at such time as the government presents evidence to this court:

> "a. that the methods used in and the facilities and controls used by the defendants for the manufacture, processing, packing and holding of drugs do not conform to and are not operated in conformity with current good manufacturing practices, or
>
> b. that any drug manufactured by the defendants is found by the government to be adulterated or misbranded within the meaning of the law, provided that all administrative proceedings be exhausted; . . . ."

[3] The court recited in its 1969 Order of Permanent Injunction that both defendants had appeared; that the court had heard testimony and received evidence; that it had issued Findings of Fact and Conclusions of Law; and that the defendants had consented to the entry of a Permanent Injunction. No appeal was taken.

It seems obvious, if there is ever to be progress in litigation,[4] that the issue before the court on the motion to reinstate was a narrow one: whether there were present any of the conditions provided in the June 29, 1970, order as causing a reversion of the injunction. That was all. The government did not have to retry its earlier case, nor reprove jurisdiction.

At the hearing the government more than met its burden. We have reviewed the complete and careful findings of the district court; they are supported by substantial evidence. They establish that the appellants' methods, facilities and controls used for the manufacture, processing, packing and holding of vitamin K (Menadione Sodium Bisulfite) injection, a drug within the meaning of 21 U.S.C. § 321(g), did not conform to current good manufacturing practices. They further establish misbranding and adulteration of the same drug within the meaning of the Act. As provided in the consent order of June 29, 1970, any of these findings justified reinstatement of the earlier injunction.

Only after the hearing did appellants raise "jurisdictional" objections, based primarily upon the government's failure to show that the vitamin K for injection entered interstate commerce after manufacture. The short answer is that the government had no reason at the hearing to try to do so. Jurisdiction had long before been settled —by the district court's 1969 findings that drugs were distributed, and components received, in interstate commerce, from which the appellants did not appeal, and by the consented-to order of permanent injunction which

[4] The June 29, 1970 order followed a hearing on June 11, 1970 at which counsel for appellants stated, in part, that "we [the Assistant United States Attorney and himself] have been conferring about the case and we have come to the stipulation as pointed out to the effect there would be a reinstatement of the injunction if in the future it is found that the operation of Dianovin Pharmaceuticals did not comply with the law as he has pointed out."

recited that the court "has jurisdiction of the subject matter herein and of all persons or parties hereto." We do not say that the injunction could be reinstated by showing the mishandling of some previously unmentioned drug over which the court clearly lacked jurisdiction. But Menadione Sodium Bisulfite injection was one of the drugs complained of in the original 1969 proceeding, where jurisdiction was conceded. The government, on its reinstatement motion, had no duty whatever to reestablish the interstate connections of the drug; at very most, if appellants, at this late date, had wished to raise a jurisdictional defense, the burden of proving the necessary facts was theirs.

Even, however, on the conceded facts relating to the interstate connections of vitamin K for injection, appellants' jurisdictional argument fails. It is undisputed that the raw material vitamin K utilized in the production of vitamin K injectible was received in interstate commerce. Following a commonly-known formula, appellants would mix the ingredients with liquid and place the resulting solution in ampules for sale. Adulteration or misbranding resulting from the doing of an act "with respect to, a . . . drug . . . , if such act is done while such article is held for sale (whether or not the first sale) after shipment in interstate commerce" is a prohibited act. 21 U.S.C. § 331(k). Apart from the fact that the end product—vitamin K for injection—was a drug, as defined in 21 U.S.C. § 321(g)(1), being in the National Formulary, its component raw materials were likewise drugs, being "articles intended for use as a component" of such a drug. 21 U.S.C. § 321(g)(1)(D). We see no point in restating the principles we recently set forth in *United States* v. *Cassaro, Inc.*, 443 F.2d 153 (1st Cir. 1971). Although dealing with flour held after interstate shipment (which the defendant made into

bread and rolls for local sale), the case is controlling.[5] The appellants' use of components shipped in interstate commerce to make vitamin K for injection brought their activities within § 331(k), and conferred jurisdiction to restrain violations thereof upon the district court. 21 U.S.C. § 332. As in *Cassaro,* we see nothing in § 331(k) or the district court's action transgressing the proper limits of authority conferred by the Commerce Clause.

The district court already having subject matter jurisdiction under the prior proceeding, and the appellants' most recent improper activities being related to a drug within the court's jurisdiction, it could plainly reinstate the original injunction for breach of the conditions of its suspension.

Appellants' "new drug" argument is of no help to them. *See* 21 U.S.C. § 321(p). All drugs whether old or new are subject to the prohibition against adulteration or misbranding. *See* 21 CFR 1.106(b)(3)(ii) for special labelling requirements applicable to prescription new drugs. The issue is irrelevant to reinstatement of the injunction. The same may be said of appellants' last-minute attempt to attack the terms of the injunction. It is the same injunction entered without appeal and with their consent in 1969. Through counsel they agreed in 1970 that it could be reinstated upon a showing of the activities which were here abundantly demonstrated. The evidence of seriously deficient conditions and practices at appellants' plant, coupled with a history of unsuccessful efforts to obtain compliance

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[5] *See also United States* v. *39 Cases . . . Mich. Brand Korleen Tablets,* 192 F.Supp. 51 (E.D. Mich. 1961), *aff'd sub nom. United States* v. *Detroit Vital Foods, Inc.,* 330 F.2d 78 (6th Cir. 1964), *cert. den.* 379 U.S. 832 (1964); *United States* v. *40 Cases . . . Pinocchio Brand 75% Corn . . . Oil,* 289 F.2d 343 (2nd Cir. 1961), *cert. den.* 368 U.S. 831 (1961); *Palmer* v. *United States,* 340 F.2d 48 (5th Cir. 1964), *cert. den.* 382 U.S. 903 (1965); *United States* v. *Allbrook Freezing & Cold Storage, Inc.,* 194 F.2d 937 (5th Cir. 1952).

by appellants with laws designed to protect the health and lives of the public, more than warranted injunctive relief. *See United States* v. *Diapulse Corporation of America*, 457 F.2d 25, 28-29 (2nd Cir. 1972). We find no attempt to impose "colonial rule" upon Puerto Rico, as appellants suggest. To the contrary, were the citizens of Puerto Rico to be denied the protection of food and drug laws, enacted for the safety of all United States citizens, wherever residing, they could quite properly complain.

Affirmed. Costs to appellee.

APPENDIX B

IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF PUERTO RICO

Civil No. 43-69

UNITED STATES OF AMERICA
PLAINTIFF
v.
DIANOVIN PHARMACEUTICALS, INC.,
a corporation, and NICOLAS O.
CABRERO ORONOZ, an individual,
DEFENDANTS.

ORDER

On February 17, 1969, this Court granted an Order of Permanent Injunction against Dianovin Pharmaceuticals, Inc. and Nicolas O. Cabrero Oronoz, defendants in the present proceeding, generally prohibiting defendants from manufacturing or introducing into interstate commerce drugs manufactured by the defendants in violation of the Federal Food, Drug and Cosmetic Act. On June 29, 1970, plaintiff, United States of America and defendants, both requested that the referred to injunction be suspended. However, both parties agreed that the injunction would revert to its full force and effect if defendants were to commit any of the following acts:

(1) that the methods used in and the facilities and controls used by the defendants for the manufacture processing, packing and holding of drugs do not conform to and are not operated in conformity with current good manufacturing practices; or

(2) that any drug manufactured by the defendants is found by the Government to be adulterated or misbranded within the meaning of the law.

The plaintiff, on February 5, 1971, moved that this Court reinstate the terms of the permanent injunction, alleging that defendants' manufacturing of drugs did not conform to good manufacturing practices and that drugs manufactured by the defendants were found to be adulterated or misbranded within the meaning of the law.

Evidentiary hearings on the Government's motion were held on May 4, 5 and 6, 1971. On July 28, 1971, defendants filed a Motion for Dismissal alleging lack of jurisdiction under Sections 331 and 332 of Title 21, United States Code.

On the basis of the foregoing, the files and record in the above captioned cause, and after considering the evidence which was introduced by the parties herein, and reviewing the memoranda submitted, and otherwise being duly advised on the premises, the Court makes the following:

Findings of Fact

1. That Vitamin K for injection, otherwise known as Menadione Sodium Bisulfite Injection, is listed in the National Formulary.

2. That the National Formulary requires that sterile ampules for injection be packed in such a manner as to prevent contamination or loss of contents.

3. That on November 25, 1970, December 3, 1970 and January 8, 1971, representative samples of ampules of Vitamin K for injection, manufactured by defendants and identified as Lots 70-12 and 70-19, were collected from defendants' finished products storeroom. The ampules were tested by United States Food and Drug Analysts for completeness of closure by visual examination after their immersion in a dye solution. A significant number of the ampules were found to have permitted the dye to become mixed with the drug, showing incomplete closure of the ampules.

4. That on January 15, 1971, a sample consisting of

approximately 500 ampules of Vitamin K for injection, manufactured by defendants and bearing the Lot number 7-12, was collected from the Ponce District Hospital. Of those tested for leakage of the drug, 5% were found to allow loss of their contents.

5. Inspection of the Dianovin Pharmaceutical plant by United States Food and Drug Administrators on November 25, 26, 27 and December 3, 1979, revealed numerous deficiencies in the methods, facilities and controls employed by the defendants for the manufacture, processing, packing, labeling and distribution of drugs, including sterile Vitamin K for injection:

(a) batch records for several drugs contained unexplained and unendorsed changes in the amounts of chemicals from that shown on the master formula, failed to indicate the ph measurement of the drug or that such a test was over performed, failed to make any comparison between theoretic and actual batch yield, did not bear the date of the drug's sterilization.

(b) a number of broken or open windows were found in, or immediately adjacent to, the area in which sterile drugs for injection are produced.

(c) environmental testing for contamination carried out in the drug filling room indicated the presence of as many as sixteen bacterial colonies on days when filling operations for sterile drugs were being carried out, and the firm's records failed to indicate any testing of the filling room during one day of its use.

(d) the defendant, Nicolas O. Cabrero, was observed without a head covering while engaged in the manufacture of a sterile drug for injection.

(e) no system of label accountability exists or is employed in the firm's labeling operations and loose labels were found lying on shelves in the labeling area. There was no record that printing plates used in the labeling

of vials and ampules were examined for accuracy after their receipt from the manufacturers, and a number of ampules of drugs had been left in the manufacturing area identified only by a piece of unattached paper.

6. The batch record of a drug is intended to provide a precise manufacturing history of any particular batch or lot of a drug, and a step by step record of the exact manner and conditions under which that drug was produced, including the amounts and strength of each component, results of both inproduction and finished product testing, amount of drug actually produced and amount expected to be produced, and the dates on which each step in the process was accomplished. Each separate recording must bear the initials of the individual to insure that the step and its recordation are correct. The absence of any one of the above types of data makes it impossible to assure that errors have not been committed and that the batch of drugs was manufactured, processed, or packed in the proper manner.

7. The physical condition of the building or facility in which drugs are manufactured, processed, packed or held, is a major factor of current good manufacturing practices, especially with respect to sterile drugs for injection. Unless such facilities are adequate and are properly maintained, controls and procedures intended to assure that the drug is free from contamination are likely to be ineffective.

Any broken or open windows in or adjacent to production areas leading to the outside of the building, significantly increase the contamination of the environment and increase the chances of contamination of the filling room and the finished product. Environment testing of both the filling room and adjacent areas is indicative of the effectiveness of contamination controls, and in the absence of such tests there is no assurance that the at-

mosphere and any drug filled under these conditions is not contaminated by micro-organisms. The environment of the room in which sterile drugs are filled must be tested on each day in which the drug is filled, and if the tests show more than one bacterial colony, the drug must be destroyed or resterilized. The presence of thirteen colonies on one settling plate evidences that the controls and procedures are of little effect, and that the room is contaminated.

8. Procedures for the labeling of drugs must be such that each label is specifically accounted for both prior and subsequent to the labeling operation for each batch of drug. Unless such an accountability system is in effect, and labels for use on different drugs or different batches of the same drug are not permitted to be left lying loosely about, an incorrect label may be used. For the same reason, it is essential that batches of drugs are properly identified throughout their production. Identification by means of unattached papers which are easily lost, misplaced or destroyed, does not assure proper identification. And, where label printing plates are used to print the label directly onto the ampules, unless the plates are examined for accuracy prior to use and a record made of such examination, there can be no assurance that the label will not contain an error.

In view of the above Findings of Fact, the Court makes the following:

Conclusions of Law

1. This Court has jurisdiction over the subject matter herein and of all persons or parties hereto, pursuant to Paragraph 1 of the Order of Permanent Injunction, dated February 17, 1969, and to the Order of Suspension, dated June 29, 1970. Section 332 of Title 21, United States Code, grants the district courts of the United States jurisdiction over violations of Section 331 of the Federal Food,

Drug and Cosmetic Act, Title 21, United States Code. Subparagraph (b) prohibits the adulteration or misbranding of any food, drug, device or cosmetic in interstate commerce. Defendants allege that since the product that they manufacture is sold only locally within the Commonwealth of Puerto Rico, they are not engaged in interstate commerce. Defendants concede in their Brief in Support of Motion for Dismissal that the raw material Vitamin K utilized in the production of Vitamin K injectible, is received from outside Puerto Rico. It is enough that the active ingredient of a drug be shipped in interstate commerce to satisfy the interstate commerce requirement of the Federal Food, Drug and Cosmetic Act. *Palmer* v. *United States,* 340 F.2d 48 (5 Cir., 1964); *United States* v. *Detroit Vital Foods, Inc.,* 330 F.2d 78 (6 Cir., 1964); *United States* v. *40 Cases* . . . ,289 F.2d 343 (2 Cir., 1961).

2. Vitamin K, or Menadione Sodium Bisulfite Injection, manufactured by defendants, is a drug within the meaning of Section 321(g), Title 21, United States Code, since it is included in the National Formulary.

3. Under the provisions of 21 United States Code 352 (g), a drug is deemed to be misbranded if it purports to be a drug the name of which is recognized in an official compendium, unless it is packaged as prescribed in such compendium. Vitamin K for injection is such a drug recognized in the National Formulary. Ampules of lots 70-12 and 70-19 of Vitamin K for injection, manufactured by the defendants were not completely sealed, and the lots are, therefore, in violation of 21 United States Code 352(g) in that they failed to comply with the standard of packaging for sterile drugs for injection prescribed by the National Formulary.

4. Under the provisions of 21 United States Code 351(a)(2)(B), a drug is adulterated if the methods used in, or the facilities and controls used for its manufactur-

ing, processing, packing or holding do not conform to or are not operated or administered in conformity with current good manufacturing practice to assure that such drug meets the requirement of the Act as to safety, and has the identity and strength, and meets the quality and purity characteristics which it purports or is represented to possess. Sections 133.2 to 133.14 of 21 C.F.R., define and interpret the meaning of "good manufacturing practices". Said regulations contain the criteria for determining whether the methods used in, or the facilities or controls used for, the manufacture, processing, packing, or holding of a drug conform to or are operated or administered in conformity with current good manufacturing practice. *United States* v. *Bel-Mar Laboratories, Inc.,* 284 F. Supp. 875, at 883 (D.C. N.Y., 1968). We find that defendants, on various grounds, have violated Section 331, Title 21 United States Code, as defined in Section 351 (a)(2)(b) and 21 C.F.R. 133.2-133.14.

21 C.F.R. 133.3, requires that buildings in which drugs are manufactured be maintained clean and contain adequate bacteriological controls. It is evident that defendants did not comply with this requirement since as many as sixteen bacterial colonies were found to have existed in the defendants' filling room on days when filling operations were carried out. The fact that several broken windows were found in or immediately adjacent to areas in which sterile drugs are produced, also adequately substantiates the Government's claim. The expert testimony presented by plaintiffs, reveals the seriousness of these two violations. As few as one bacterial colony present in an area where drugs are produced, would justify the destruction of a lot produced under those conditions. The physical integrity of a building constitutes a primary barrier against bacteria. Broken windows permit bacteria to easily overcome this defense line.

Sections 133.7(a)(3) and 133.7(b)(1), require that master formula records be prepared for each drug product and that a complete batch formula be produced from the master formula record for each batch of product to be produced. Several of defendants' batch records contained unexplained and unendorsed changes in the amounts of chemicals from that shown on the master formula.

Defendants also failed to make any comparison between theoretic and actual batch yield. Sections 133.7(a)(3) and 133.8(f), clearly establish that this practice does not conform to the good manufacturing practices definition of the Federal Food, Drug and Cosmetic Act.

Defendant Cabrero was observed without a head covering while engaged in the manufacture of a sterile drug for injection. Section 133.6, 21 C.F.R., requires that components used in the manufacture of drugs be handled in such a way as to prevent contamination. There is ample expert testimony in the record to conclude that it is essential that personnel involved in the mixing and production of sterile drugs must wear head covers, since hair constitutes one of the body's protective agents against bacteria, by collecting bacteria and thus constituting a possible source of contamination in the mixing and production aspects of the manufacture of sterile drugs.

Defendants failed to record the measurement of the P.H. factor in the manufacture of liquid products or to detail what measures they undertook to control, eliminate or otherwise deal with it in the batch sheets. The P.H. factor is a measurement of hydrogen iron concentration which is essential since P.H. may affect the characteristics of the drug. This is also a violation of Section 133.7 which requires a complete detail in the batch sheets of the important steps in the manufacturing process of finished pharmaceuticals.

Maintaining a complete record of the steps involved in sterilizing drugs is an essential element in the production

and manufacture of sterile parenteral drugs. Defendants omitted to include in their batch records, the dates on which sterilization of the drugs they manufacture were carried out. On one occasion the firm's records failed to indicate any testing of the filling room for sterility during one day of its use. Both these incidents constitute violations of Sections 133.7 and 133.6 which require that records be maintained to cover the essential elements or steps in the manufacturing process.

There is sufficient evidence to establish that defendants maintained no system of label accountability, that loose labels were found lying on shelves in the labeling area, and that at least, on one occasion a number of ampules of drugs had been left in the manufacturing area identified only by a piece of unattached paper. It was also found that no record that printing plates used in the labeling of vials and ampules were examined for accuracy after their receipt from the manufacturer. All these facts do not conform to the good manufacturing practices contained in Section 133.10, 21 C.F.R., with respect to packaging and labelling, and in Section 133.8(b), which requires that drugs be stored and handled in such a way as to prevent mixups with other drugs.

5. We hereby find, therefore, that drugs manufactured by the defendants are both adulterated and misbranded in violation of the law, and not manufactured, processed, packed and held in conformity with current good manufacturing practices.

It is, therefore, ORDERED, that this Court's Order suspending the terms and conditions of the Permanent Injunction, dated June 29, 1970, is vacated, and the Order of Permanent Injunction shall revert to its full force and effect.

It is, therefore, further ORDERED, as follows:

1. That the defendants, Dianovin Pharmaceuticals, Inc.,

a corporation, and Nicolas O. Cabrero Oronoz, an individual, and each and all of their officers, agents, servants, employees, and representatives and any and all other persons in active concert or participation with them or any of them, be perpetually restrained and enjoined from directly or indirectly doing or causing to be done any of the following acts:

A. introducing and delivering for introduction into interstate commerce, in violation of 21 U.S.C. 331(a), any article of drug manufactured, processed, packed or labeled by said defendants:

(a) which is adulterated within the meaning of 21 U.S.C. 351(a)(2)(b) in that the methods used in and the facilities and controls used for its manufacture, processing, packing and holding do not conform to and are not operated and administered in conformity with current good manufacturing practice to assure that such drug meets the requirements of the Federal Food, Drug, and Cosmetic Act as to safety and has the identity and strength and meets the quality and purity characteristics which it purports and is represented to possess;

(b) which is adulterated within the meaning of 21 U.S.C. 351(b) in that it purports to be or is represented as a drug the name of which is recognized in an official compendium and its strength differs from or its quality or purity falls below the standard set forth in the official compendium;

(c) which is adulterated within the meaning of 21 U.S.C. 351(c) in that it is not subject to 21 U.S.C. 351(b) and its strength differs from or its purity or quality falls below that which it purports or is represented to possess;

(d) which is misbranded within the meaning of 21 U.S.C. 352(a) in that the statements appearing on the

labeling of the article of drug are false and misleading in regard to the identity, strength, purity or quality of the article of drug;

(e) which is misbranded within the meaning of 21 U.S.C. 352(f)(1) in that the labeling of the article of drug fails to bear adequate directions for use and it is not exempt from such requirement since it is a drug subject to the requirements of 21 U.S.C. 353(b)(1) and its labeling fails to bear, as required by regulations 21 C.F.R. 1.106(b)(3)(i), adequate information for its use under which practitioners licensed by law to administer such drug could use such drug safely and for the purposes for which it was intended; or

(f) which is misbranded within the meaning of 21 U.S.C. 353(b)(4) in that the article of drug is subject to 21 U.S.C. 353(b)(1) and its label fails to bear the statement "Caution: Federal law prohibits dispensing without prescription".

B. manufacturing, processing, packing, or labeling, in violation of 21 U.S.C. 331(k), any article of drug while held for sale after shipment of one or more of its components in interstate commerce, which act of manufacturing, processing, packing, or labeling, results in such article of drug being adulterated or misbranded as set forth hereinabove in subparagraph (A); and

C. introducing and delivering for introduction into interstate commerce, in violation of 21 U.S.C. 331(a), any article of drug manufactured, processed, packed, or labeled at said defendants' plant at Santurce, Puerto Rico, and manufacturing, processing, packing or labeling at said plant, in violation of 21 U.S.C. 331(k), any article of drug while held for sale after shipment of one or more of its components in interstate commerce, unless and until:

(1) methods, facilities and controls for manufacturing, processing, packing, labeling, and holding such

article of drug at said plant are established and operated and administered in conformity with good manufacturing practice (21 C.F.R. 133.1 - .14), which methods, facilities and controls shall specifically include the following:

(a) receipt of raw materials is properly documented and containers thereof are properly identified;

(b) raw materials and finished products are properly tested for identity, strength, quality and purity;

(c) a quarantine area for raw materials is established and maintained;

(d) master formula records and batch production records are dated and endorsed by two competent individuals;

(e) batch production records list the batch number;

(f) batch production records are made out for all batches;

(g) action is taken to assure the sterility of all parenteral drugs including adequate sterility testing thereof;

(h) pyrogen testing is conducted on all products which are required to be pyrogen free;

(i) bacterial plate counts are made of the sterile fill room;

(j) the vial and ampul filling rooms have positive air pressure and are supplied with filtered air;

(k) the vial and ampul filling room openings leading to the outside of the building are closed;

(l) the ceiling of the vial and ampul filling room is made so that it can be sanitized;

(m) gowns used by personnel employed in the vial and ampul filling rooms are autoclaved;

(n) the dressing room for personnel employed in the vial and ampul filling rooms is changed so that such personnel will not be required to enter the vial filling room to get to the dressing room;

(o) the entry of employees into the vial filling room in their street clothes and shoes is discontinued;

(p) the hood used for filling vials is fixed so that it can be sanitized properly;

(q) accountability is made of all labels used in the labeling operations;

(r) stability tests are performed on all products subject to deterioration after manufacture;

(s) lot numbers of the products distributed are listed on the invoices of such products;

(t) reserve samples of the finished products are retained.

(2) duly authorized Food and Drug Inspectors are granted free access to said plant for the purpose of making an inspection of such plant including the building, pertinent equipment, finished and unfinished materials, containers, labeling, and all records relating to the methods used in, and the facilities and controls used for, the manufacture, processing, packing and holding of drugs, and such inspection shows that the established methods, facilities and controls appear to be operated and administered in conformity with current good manufacturing practice, the cost of any such inspection to be borne by the defendants at the rate of $8.00 per hour and fraction thereof per representative for inspectional work, $10.00 per hour and fraction thereof per representative for laboratory and

analytical work and $27.00 per day per person for subsistence expenses where necessary; and

(3) all of the drugs manufactured, processed, packed or labeled at said plant at Santurce, Puerto Rico, which are on hand in the possession of the said defendants are either destroyed, reworked, or otherwise brought into compliance with the law under the supervision of the Food and Drug Administration, and all expenses are paid by the said defendants at the rates hereinbefore specified.

2. That the defendants, Dianovin Pharmaceuticals, Inc., a corporation, and Nicolas O. Cabrero Oronoz, an individual, shall give written notice of the provisions of this decree to each and all of their officers, agents, servants, employees, representatives, and any and all persons now or in the future in active concert or participation with them or any of them who assist or participate in the manufacture and distribution of articles of drug.

3. That jurisdiction of this Court is retained for the purpose of enforcing or modifying this decree for the purpose of granting such additional relief as may hereafter appear necessary or appropriate.

San Juan, Puerto Rico, May 1st., 1972.

(s) JOSE V. TOLEDO
JOSE V. TOLEDO
U. S. District Judge